II. REMARKS:

A. Status of the Claims

Claims 1-4 were originally filed with the present case, which is a continuation-in-part of U.S. application serial no. 09/308,295, filed May 17, 1999, now abandoned. Claims 1-4 were subject to a Restriction Requirement mailed on June 29, 2006. Applicants elected the Group I invention (Claims 1-3) in a Response to Restriction Requirement filed on July 28m 2006. Claims 1-3 are rejected herein. Claim 1 is amended, claims 2 and 3 are canceled, and claim 4 is withdrawn as being directed to a non-elected invention. No claims are added herein.

B. The Claims are Definite and Enabled

The Action rejects claims 1-3 as being indefinite for failing to particularly point out the subject matter of the invention. The Action states that it is not clear what is "aberrant expression of GRβ" so as to allow the metes and bounds of the claim to be determined. The Action further asserts that it is not clear what "defect in the GRβ isolated from said sample" alters the degree of alternative splicing so as to allow the metes and bounds of the claim to be determined. Claim 3 is also said to be unclear as omitting essential steps required to identify the defect in the GRβ isolated from the sample. The Action further rejects the claims for lacking enablement. The Action acknowledges that the claims are enabling for a method for diagnosing glaucoma in a patient wherein a decrease in GRβ expression in the trabecular meshwork as compared to the expression of GRβ of a non-glaucomatous patient indicates a diagnosis of glaucoma. Nonetheless, the Action argues that the specification is not enabling for other methods of diagnosing glaucoma in a patient. The Action asserts that the specification, claims or prior art do

not state how to use the assays described to specifically diagnose glaucoma. Applicants respectfully traverse.

Applicants reiterate that a patent need not disclose what is well known in the art. *In re Wands*, 858 F.2d 731, 735, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986) (citing *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984)). In this case, the artisan skilled in the field of diagnosis of diseases using genetic information would be well aware of the techniques for detection of genetic expression and defects in a gene and would understand the phrases "aberrant expression", and "defects in the GRβ." Moreover, the skilled artisan would be able to make the connection between such aberrant expression in the trabecular meshwork and a diagnosis of glaucoma.

There are a number of techniques commonly used to detect variations in DNA sequences, and these are often used to screen for possible gene mutations. These techniques are well known by those skilled in the art (for example see Birren *et al.*, 1998; pp287-384 and Strachan & Read, 1996; pp. 367-399). Among the electrophoretic mobility alteration methods described in Birren (*see* Table 1, p. 289; attached hereto as Exhibit A) are: single-strand confirmation polymorphism (SSCP), denaturing gradient gel electrophoresis (DGGE), restriction enzyme fingerprinting, chemical cleavage of mismatches (CCM), constant denaturant gel electrophoresis (CDGE), and nondenaturing gel mismatch detection.

In SSCP, specific regions of normal and disease genes are amplified by PCR and loaded onto nondenaturing polyacrylamide gels. Single stranded DNA folds upon itself, and its electrophoretic migration is based on its sequence and length. Changes in DNA sequence are often identified by alterations in the DNA fragment mobility. DNA sequencing of fragments with altered mobilities identifies specific nucleotide changes. Thus, clearly SSCP is a method, known by those skilled in the art, that can detect a single nucleotide change through altered gel electrophoretic mobility.

Nevertheless, simply to progress the case toward allowance, Applicants have amended claim 1 to specify that a decrease in expression of GRβ in glaucomatous tissues as compared to the expression of GRβ in non-glaucomatous tissues leads to a diagnosis of glaucoma. Claims 2 and 3 are canceled to focus on the aberrant expression aspect of the invention at this time. Applicants reserve the right to pursue the subject matter contained within claims 2 and 3 in a later filed continuation application. It is believed that the amendments to the claims renders the definiteness and enablement rejections moot.

In light of the foregoing arguments, Applicants submit that the claims are definite and enabled and therefore, respectfully request that such rejections be withdrawn.

C. Conclusion

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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